



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 108474

TO: Devesh Khare
Location: cm1/8a13/8b19
Art Unit : 1623
Tuesday, November 18, 2003

Case Serial Number: 10/007489

From : Susan Hanley
Location: Biotech-Chem Library
CM1 6B05
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Enter your Contact Information below:

Name:

Devesh Khare

Employee Number: 77931

Phone:

605-1199

Art Unit or Office: 1623

Building & Room Number:

8 A 13, Mail 8 B19

Enter the case serial number (Required): 10/007,489

If not related to a patent application, please enter NA here.

Class / Subclass(es) 536/25.34

Earliest Priority Filing Date: 09/14/1998

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Provide detailed information on your search topic:

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- *For Chemical Structure Searches Only*
Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers

108474

- ***For Sequence Searches Only***
Include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.
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- Provide examples or give us relevant citations, authors, etc., if known.
- FAX or send the **abstract, pertinent claims** (not all of the claims), **drawings, or chemical structures** to your EIC or branch library.

Enter your Search Topic Information below:

Please search the following claims:

Claim 1: A method for generating phosphorothioate oligo mixtures comprising:

- 1) growing a single-stranded recombinant DNA phage in modified media that uses thio-phosphate as a source of phosphate
- 2) harvesting the single-stranded phage and purifying the DNA corresponding to the recombinant DNA insert
- 3) fragmentation of the insert DNAsuch that oligo mixtures spanning the entire length of the segment are generated

Claim 2: the method of claim 1 used to generate phosphorothioate ds DNA, ss DNA, and/or RNA by in vivo incorporation of thio-phosphate into nucleotide precursor pools.

Thank you.
devesh khare

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Last Modified: Wednesday, December 31, 1969 19:00:00

007, 489

=> file medline

FILE 'MEDLINE' ENTERED AT 14:47:28 ON 18 NOV 2003

FILE LAST UPDATED: 13 NOV 2003 (20031113/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See <http://www.nlm.nih.gov/mesh/changes2003.html> for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que 158

L55 546 SEA FILE=MEDLINE ABB=ON PLU=ON 10101-88-9 OR THIOPHOSPHORIC
OR 13598-51-1
L56 3 SEA FILE=MEDLINE ABB=ON PLU=ON L55 AND (SSDNA OR SINGLE-STRAN
D? OR SS DNA)
L57 2090 SEA FILE=MEDLINE ABB=ON PLU=ON ORGANOTHIOPHOSPHORUS COMPOUNDS
/CT
L58 1 SEA FILE=MEDLINE ABB=ON PLU=ON L56 AND L57

=> file embase

FILE 'EMBASE' ENTERED AT 14:47:29 ON 18 NOV 2003

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FILE COVERS 1974 TO 13 Nov 2003 (20031113/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que 173

L64 962 SEA FILE=EMBASE ABB=ON PLU=ON 10101-88-9 OR THIOPHOSPHORIC
OR 13598-51-1 OR THIOPHOSPHATE
L65 69 SEA FILE=EMBASE ABB=ON PLU=ON L64 AND (SSDNA OR SINGLE-STRAND
? OR SS DNA OR ?PHAGE OR PLASMID)
L66 38 SEA FILE=EMBASE ABB=ON PLU=ON L65 AND ?OLIGO?
L70 15 SEA FILE=EMBASE ABB=ON PLU=ON L66 AND (HIGH OR THIOPHOSPHATE
OR PHOSPHOROTHIOATE OR EXTENDING)/TI
L71 3 SEA FILE=EMBASE ABB=ON PLU=ON L70 NOT (CHIRAL OR EFFECT OR
VIRAL OR VIVO OR ANTIPARALLEL OR SFII OR MICE OR MACROPHAGE
OR GENE OR CPC)/TI
L72 1 SEA FILE=EMBASE ABB=ON PLU=ON L66 AND EXTENDING/TI
L73 4 SEA FILE=EMBASE ABB=ON PLU=ON L71 OR L72

=> file hcaplus

FILE 'HCAPLUS' ENTERED AT 14:47:30 ON 18 NOV 2003

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FILE COVERS 1907 - 18 Nov 2003 VOL 139 ISS 21

FILE LAST UPDATED: 17 Nov 2003 (20031117/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que 110

```

L1 (      1813)SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHOROTHIOATE OLIGONUCLEOTI
          DES+PFT,NT/CT
L2      231 SEA FILE=HCAPLUS ABB=ON PLU=ON L1(L)PREP/RL
L4      5 SEA FILE=REGISTRY ABB=ON PLU=ON 03PS/MF
L5      8754 SEA FILE=REGISTRY ABB=ON PLU=ON "PHOSPHOROTHIOATE"
L6      448 SEA FILE=REGISTRY ABB=ON PLU=ON L5 AND M/ELS
L7      35 SEA FILE=REGISTRY ABB=ON PLU=ON L6 NOT C/ELS
L8      40 SEA FILE=REGISTRY ABB=ON PLU=ON L4 OR L7
L9      354 SEA FILE=HCAPLUS ABB=ON PLU=ON L8
L10     2 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND L2

```

=> d que 119

```

L3      1813 SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHOROTHIOATE OLIGONUCLEOTI
          DES+PFT,NT/CT
L4      5 SEA FILE=REGISTRY ABB=ON PLU=ON 03PS/MF
L5      8754 SEA FILE=REGISTRY ABB=ON PLU=ON "PHOSPHOROTHIOATE"
L6      448 SEA FILE=REGISTRY ABB=ON PLU=ON L5 AND M/ELS
L7      35 SEA FILE=REGISTRY ABB=ON PLU=ON L6 NOT C/ELS
L8      40 SEA FILE=REGISTRY ABB=ON PLU=ON L4 OR L7
L9      354 SEA FILE=HCAPLUS ABB=ON PLU=ON L8
L16     222353 SEA FILE=HCAPLUS ABB=ON PLU=ON DNA+PFT/CT
L17     5268 SEA FILE=HCAPLUS ABB=ON PLU=ON L16(L)(SS OR SINGLE-STRAND?)
L18     24 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND L3
L19     1 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND L18

```

=> d que 123

```

L3      1813 SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHOROTHIOATE OLIGONUCLEOTI
          DES+PFT,NT/CT
L16     222353 SEA FILE=HCAPLUS ABB=ON PLU=ON DNA+PFT/CT
L17     5268 SEA FILE=HCAPLUS ABB=ON PLU=ON L16(L)(SS OR SINGLE-STRAND?)
L18     24 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND L3
L20     486562 SEA FILE=HCAPLUS ABB=ON PLU=ON (MONOTHIO? OR PHOSPHOROTHIO?
          OR THIO? OR PHOSPHOROMONOTHIO?)
L21     24 SEA FILE=HCAPLUS ABB=ON PLU=ON L20 AND L18
L22     3 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 AND (PHAGE OR BACTERIOPHAG
          E)
L23     2 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 NOT CIRCULAR/TI

```

=> d que 125

```

L1 (      1813)SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHOROTHIOATE OLIGONUCLEOTI
          DES+PFT,NT/CT
L2      231 SEA FILE=HCAPLUS ABB=ON PLU=ON L1(L)PREP/RL
L16     222353 SEA FILE=HCAPLUS ABB=ON PLU=ON DNA+PFT/CT
L17     5268 SEA FILE=HCAPLUS ABB=ON PLU=ON L16(L)(SS OR SINGLE-STRAND?)
L24     12 SEA FILE=HCAPLUS ABB=ON PLU=ON L2 AND (PHAGE OR BACTERIOPHAGE
          )
L25     2 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 AND L17

```

=> d que 141

```

L4      5 SEA FILE=REGISTRY ABB=ON PLU=ON 03PS/MF
L5      8754 SEA FILE=REGISTRY ABB=ON PLU=ON "PHOSPHOROTHIOATE"
L6      448 SEA FILE=REGISTRY ABB=ON PLU=ON L5 AND M/ELS
L7      35 SEA FILE=REGISTRY ABB=ON PLU=ON L6 NOT C/ELS
L8      40 SEA FILE=REGISTRY ABB=ON PLU=ON L4 OR L7
L9      354 SEA FILE=HCAPLUS ABB=ON PLU=ON L8
L32     354 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND L5
L33     11 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 AND SINGLE-STRAND?
L39     10 SEA FILE=HCAPLUS ABB=ON PLU=ON L33 AND ?OLIGO?
L40     10 SEA FILE=HCAPLUS ABB=ON PLU=ON L39 AND ?THIO?
L41     7 SEA FILE=HCAPLUS ABB=ON PLU=ON L40 NOT (GOLD OR DOUBLE OR
          HAPLOTYPES)/TI

```

=> s 110 or 119 or 123 or 125 or 141

L74 12 L10 OR L19 OR L23 OR L25 OR L41

=> dup rem 158 173 174

FILE 'MEDLINE' ENTERED AT 14:47:58 ON 18 NOV 2003

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PROCESSING COMPLETED FOR L58

PROCESSING COMPLETED FOR L73

PROCESSING COMPLETED FOR L74

L75 17 DUP REM L58 L73 L74 (0 DUPLICATES REMOVED)

ANSWER '1' FROM FILE MEDLINE

ANSWERS '2-5' FROM FILE EMBASE

ANSWERS '6-17' FROM FILE HCAPLUS

=> d ibib abs ind 1-5

L75 ANSWER 1 OF 17 MEDLINE on STN

ACCESSION NUMBER: 85054878 MEDLINE

DOCUMENT NUMBER: 85054878 PubMed ID: 6094546

TITLE: Cleavage of phosphorothioate-substituted DNA by restriction endonucleases.

AUTHOR: Potter B V; Eckstein F

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1984 Nov 25) 259 (22) 14243-8.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198412

ENTRY DATE: Entered STN: 19900320

Last Updated on STN: 19900320

Entered Medline: 19841227

AB M13 RF DNA was synthesized in vitro in the presence of various single deoxynucleoside 5'-O-(1-thiotriphosphate) phosphorothioate analogues, and the three other appropriate deoxynucleoside triphosphates using a M13 (+)-single-stranded template, Escherichia coli DNA polymerase I and T4 DNA ligase. The resulting DNAs contained various restriction endonuclease recognition sequences which had been modified at their cleavage points in the (-)-strand by phosphorothioate substitution. The behavior of the restriction enzymes *Ava*I, *Bam*HI, *Eco*RI, *Hind*III, and *Sal*I towards these substituted DNAs was investigated. *Eco*RI, *Bam*HI, and *Hind*III were found to cleave appropriate phosphorothioate-substituted DNA at a reduced rate compared to normal M13 RF DNA, and by a two-step process in which all of the DNA is converted to an isolable intermediate nicked molecule containing a specific discontinuity at the respective recognition site presumably in the (+)-strand. By contrast, *Sal*I cleaved substituted DNA effectively without the intermediacy of a nicked form. *Ava*I, however, is only capable of cleaving the unsubstituted (+)-strand in appropriately modified DNA.

CT Check Tags: Support, Non-U.S. Gov't
Bacteriophage phi X 174: GE, genetics
Base Sequence
Binding Sites

*DNA Restriction Enzymes: ME, metabolism

*DNA, Single-Stranded: AN, analysis

DNA, Viral: AN, analysis

Deoxyribonuclease *Bam*HI

Deoxyribonuclease *Eco*RI

Deoxyribonuclease *Hind*III

*Organothiophosphorus Compounds: ME, metabolism

*Thiophosphoric Acid Esters: ME, metabolism

CN 0 (DNA, Single-Stranded); 0 (DNA, Viral); 0 (Organothiophosphorus Compounds); 0 (Thiophosphoric Acid Esters); EC 3.1.21 (DNA Restriction Enzymes); EC 3.1.21.- (Deoxyribonuclease *Bam*HI); EC 3.1.21.- (Deoxyribonuclease *Eco*RI); EC 3.1.21.- (Deoxyribonuclease *Hind*III); EC 3.1.21.- (endodeoxyribonuclease *Ava*I); EC 3.1.21.- (endodeoxyribonuclease *Sal*I)

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ACCESSION NUMBER: 96053473 EMBASE

DOCUMENT NUMBER: 1996053473

TITLE: Extending the chemistry that supports genetic information transfer in vivo: Phosphorothioate DNA,

phosphorothioate RNA, 2'-O-methyl RNA, and methylphosphonate DNA.

AUTHOR: Thaler D.S.; Liu S.; Tomblin G.

CORPORATE SOURCE: DNA RMCP, Jefferson Cancer Center, Thomas Jefferson University, 233 South 10th Street, Philadelphia, PA 19107, United States

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1996) 93/3 (1352-1356).
ISSN: 0027-8424 CODEN: PNASA6

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB DNA and RNA are the polynucleotides known to carry genetic information in life. Chemical variants of DNA and RNA backbones have been used in structure- function and biosynthesis studies in vitro, and in antisense pharmacology, where their properties of nuclease resistance and enhanced cellular uptake are important. This study addressed the question of whether the base(s) attached to artificial backbones encodes genetic information that can be transferred in vivo. **Oligonucleotides** containing chemical variants of DNA or RNA were used as primers for site-specific mutagenesis of bacteriophage f1. Progeny phage were scored both genetically and physically for the inheritance of information originally encoded by bases attached to the nonstandard backbones. Four artificial backbone chemistries were tested: phosphorothioate DNA, phosphorothioate RNA, 2'-O-methyl RNA and methylphosphonate DNA. All four were found capable of faithful information transfer from their attached bases when one or three artificial positions were flanked by normal DNA. Among oligonucleotides composed entirely of nonstandard backbones, only phosphorothioate DNA supported genetic information transfer in vivo.

CT Medical Descriptors:
*gene transfer
*nucleotide sequence
article
chemical structure
dna replication
dna synthesis
genetic code
molecular genetics
priority journal
site directed mutagenesis
structure activity relation
Drug Descriptors:
*dna
*rna
antisense oligonucleotide
oligonucleotide
phosphorothioic acid
transfer rna

RN (dna) 9007-49-2; (rna) 63231-63-0; (phosphorothioic acid) 10101-88-9, 13598-51-1, 15181-41-6; (transfer rna) 9014-25-9

L75 ANSWER 3 OF 17 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN

ACCESSION NUMBER: 93173385 EMBASE

DOCUMENT NUMBER: 1993173385

TITLE: Site-directed mutagenesis of single-stranded and double-stranded DNA by phosphorothioate approach.

AUTHOR: Olsen D.B.; Sayers J.R.; Eckstein F.

SOURCE: Methods in Enzymology, (1993) 217/- (189-217).
ISSN: 0076-6879 CODEN: MENZAU

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English

CT Medical Descriptors:
*site directed mutagenesis
article
bacteriophage t7
cell transformation
dna sequence
dna synthesis
dna template

escherichia coli
 gene mutation
 hydrolysis
 nonhuman
 nucleotide sequence
 plasmid
 polymerization
 priority journal
 Drug Descriptors:
 *double stranded dna
 *phosphorothioic acid
 *plasmid dna
 *single stranded dna
 dna polymerase
 ethidium bromide
 exodeoxyribonuclease iii
 oligonucleotide
 primer dna
 restriction endonuclease

RN (phosphorothioic acid) 10101-88-9, 13598-51-1,
 15181-41-6; (dna polymerase) 37217-33-7; (ethidium bromide) 1239-45-8;
 (exodeoxyribonuclease iii) 9037-44-9

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ACCESSION NUMBER: 90080670 EMBASE

DOCUMENT NUMBER: 1990080670

TITLE: High-efficiency oligonucleotide
 -directed plasmid mutagenesis.

AUTHOR: Olsen D.B.; Eckstein F.

CORPORATE SOURCE: Max-Planck Institut für, Experimentelle Medizin, Abteilung
 Chemie, Hermann-Rein Strasse 3,D-3400 Göttingen, Germany

SOURCE: Proceedings of the National Academy of Sciences of the
 United States of America, (1990) 87/4 (1451-1455).
 ISSN: 0027-8424 CODEN: PNASA6

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology
 029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A number of single- and double-base substitutions have been introduced
 into either the polylinker region or the lacZ gene in the plasmid
 vector pUC19. The efficiencies of these changes upon transfection of TG-1
 bacterial cells were generally 70-80%. A strategy has been devised by
 which the wild-type DNA can be selectively destroyed. It is primarily
 based on the resistance of phosphorothioate internucleotide linkages to
 some restriction enzymes. A mismatch oligonucleotide is
 introduced into a gapped region and the gap is filled using three
 deoxynucleoside 5'-triphosphates and one deoxynucleoside
 5'-[.alpha.-thio]triphosphate. Reaction with a restriction enzyme that is
 unable to hydrolyze phosphorothioates ensures that the DNA containing the
 mismatch oligonucleotide is only nicked. Concomitantly, the DNA
 that does not contain the desired mutation is linearized. Subsequent
 reactions with an exonuclease and DNA polymerase I yield mutant homoduplex
 DNA for transfection.

CT Medical Descriptors:

*plasmid
 *site directed mutagenesis
 genetic engineering
 nonhuman
 article
 priority journal
 Drug Descriptors:
 *phosphorothioic acid

RN (phosphorothioic acid) 10101-88-9, 13598-51-1,
 15181-41-6

L75 ANSWER 5 OF 17 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED.
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ACCESSION NUMBER: 90371788 EMBASE

DOCUMENT NUMBER: 1990371788

TITLE: Chemical and enzymatic ligation of 5'-
 thiophosphates of oligodeoxyribonucleotides

AUTHOR: Oshevskaia S.I.

CORPORATE SOURCE: Institute of Cytology and Genetics, Siberian Branch of the
 Academy of Sciences of the USSR, Novosibirsk, Russia

SOURCE: Doklady Biochemistry, (1990) 310/1-6 (15-18).
 ISSN: 0012-4958 CODEN: DBIOAM
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 029 Clinical Biochemistry
 LANGUAGE: English
 CT Medical Descriptors:
 bacteriophage t4
 article
 Drug Descriptors:
 *dna
 *oligonucleotide
 *rna
 RN (dna) 9007-49-2; (rna) 63231-63-0

=> d ibib abs hitrn 6

L75 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2003:461948 HCAPLUS
 DOCUMENT NUMBER: 139:225986
 TITLE: Comparison of different antisense strategies in
 mammalian cells using locked nucleic acids,
 2'-O-methyl RNA, phosphorothioates and small
 interfering RNA
 AUTHOR(S): Gruenweller, Arnold; Wyszko, Eliza; Bieber, Birgit;
 Jahnel, Ricarda; Erdmann, Volker A.; Kurreck, Jens
 CORPORATE SOURCE: Institut fuer Chemie-Biochemie, Freie Universitaet
 Berlin, Berlin, D-14195, Germany
 SOURCE: Nucleic Acids Research (2003), 31(12), 3185-3193
 CODEN: NARHAD; ISSN: 0305-1048
 PUBLISHER: Oxford University Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Locked nucleic acids (LNAs) and double-stranded small interfering RNAs
 (siRNAs) are rather new promising antisense mols. for cell culture and in
 vivo applications. Here, we compare LNA-DNA-LNA gapmer
 oligonucleotides and siRNAs with a phosphorothioate and
 a chimeric 2'-O-Me RNA-DNA gapmer with respect to their capacities to
 knock down the expression of the vanilloid receptor subtype 1 (VR1).
 LNA-DNA-LNA gapmers with four or five LNAs on either side and a central
 stretch of 10 or 8 DNA monomers in the center were found to be active
 gapmers that inhibit gene expression. A comparative co-transfection study
 showed that siRNA is the most potent inhibitor of VR1-green fluorescent
 protein (GFP) expression. A specific inhibition was obsd. with an estd.
 IC50 of 0.06 nM. An LNA gapmer was found to be the most efficient
 single-stranded antisense oligonucleotide,
 with an IC50 of 0.4 nM being 175-fold lower than that of commonly used
 phosphorothioates (IC50 .apprx.70 nM). In contrast, the
 efficiency of a 2'-O-methyl-modified oligonucleotide
 (IC50.apprx.220 nM) was 3-fold lower compared with the
 phosphorothioate. The high potency of siRNAs and chimeric LNA-DNA
 oligonucleotides make them valuable candidates for cell culture
 and in vivo applications targeting the VR1 mRNA.
 IT 15181-41-6, Phosphorothioate
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (RNA; gene silencing using locked nucleic acids, 2'-O-Me RNA,
 phosphorothioates and siRNA)
 REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitrn 7

L75 ANSWER 7 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2003:339079 HCAPLUS
 DOCUMENT NUMBER: 139:1495
 TITLE: Antisense technologies. Improvement through novel
 chemical modifications
 AUTHOR(S): Kurreck, Jens
 CORPORATE SOURCE: Institut fur Chemie-Biochemie, Freie Universitat
 Berlin, Berlin, 14195, Germany
 SOURCE: European Journal of Biochemistry (2003), 270(8),
 1628-1644
 CODEN: EJBICAI; ISSN: 0014-2956
 PUBLISHER: Blackwell Publishing Ltd.
 DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Antisense agents are valuable tools to inhibit the expression of a target gene in a sequence-specific manner, and may be used for functional genomics, target validation and therapeutic purposes. Three types of anti-mRNA strategies can be distinguished. Firstly, the use of **single stranded antisense-oligonucleotides**; secondly, the triggering of RNA cleavage through catalytically active **oligonucleotides** referred to as ribozymes; and thirdly, RNA interference induced by small interfering RNA mols. Despite the seemingly simple idea to reduce translation by **oligonucleotides** complementary to an mRNA, several problems have to be overcome for successful application. Accessible sites of the target RNA for **oligonucleotide** binding have to be identified, antisense agents have to be protected against nucleolytic attack, and their cellular uptake and correct intracellular localization have to be achieved. Major disadvantages of commonly used **phosphorothioate DNA oligonucleotides** are their low affinity towards target RNA mols. and their toxic side-effects. Some of these problems have been solved in "second generation" nucleotides with alkyl modifications at the 2' position of the ribose. In recent years valuable progress has been achieved through the development of novel chem. modified nucleotides with improved properties such as enhanced serum stability, higher target affinity and low toxicity. In addn., RNA-cleaving ribozymes and deoxyribozymes, and the use of 21-mer double-stranded RNA mols. for RNA interference applications in mammalian cells offer highly efficient strategies to suppress the expression of a specific gene.

IT 15181-41-6, Phosphorothioate

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(comparison of different antisense strategy)

REFERENCE COUNT: 131 THERE ARE 131 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitrn 8

L75 ANSWER 8 OF 17 HCAPLUS COPYRIGHT 2003 ACS ON STN

ACCESSION NUMBER: 2003:609425 HCAPLUS

DOCUMENT NUMBER: 139:241236

TITLE: A comparison of gene repair strategies in cell culture using a lacZ reporter system

AUTHOR(S): Nickerson, H. D.; Colledge, W. H.

CORPORATE SOURCE: Department of Physiology, University of Cambridge, Cambridge, UK

SOURCE: Gene Therapy (2003), 10(18), 1584-1591

CODEN: GETHEC ISSN: 0969-7128

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Synthetic **oligonucleotides** and DNA fragments of less than 1 kilobase (kb) have been shown to cause site-specific genetic alterations in mammalian cells in culture and in vivo. We have used a lacZ reporter gene system to compare the efficiency of episomal and chromosomal gene repair in human embryonic kidney epithelial cells (HEK293), Chinese Hamster Ovary fibroblasts (CHOK1), human bronchial epithelial cells (16HBE), and mouse embryonic stem (ES) cells. The lacZ gene contains a G to A nucleotide change, (Glu to Lys mutation) that abrogates .beta.-galactosidase activity. We compared the efficiency of different gene repair methods to correct this mutation and restore .beta.-galactosidase activity. We evaluated PCR-generated double-stranded DNA fragments of 0.52-1.9 kb, **single-stranded DNA oligonucleotides** of 20, 35, or 80 bases contg. internal **phosphorothioate** links, and a 68 base RNA:DNA **oligonucleotide**. All of the **oligonucleotides** and DNA fragments showed some gene repair ability with an episomal plasmid. Short DNA fragments of 0.52 kb or greater gave the highest frequencies of episomal gene repair while **single-stranded DNA oligonucleotides** gave the highest frequency of chromosomal repair. In the context of a chromosomal target, antisense DNA **oligonucleotides** gave 5-fold higher frequencies of gene repair than their sense counterparts. The RNA:DNA chimeric **oligonucleotide** gave little or no gene repair on either a chromosomal or episomal target.

IT 15181-41-6, Phosphorothioate

RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(comparison of gene repair strategies in cell culture using a lacZ

reporter system)
 REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitrn 9

L75 ANSWER 9 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2002:658292 HCAPLUS
 DOCUMENT NUMBER: 137:196646
 TITLE: Defined DNA sequences amplifiable with a universal
 primer pair for use in labeling materials for
 identification
 INVENTOR(S): Brown, Tom; Thelwell, Nichola; Maxwell, Paula;
 Maxwell, Paul; Whiting, Paul
 PATENT ASSIGNEE(S): Crime Solutions Limited, UK
 SOURCE: PCT Int. Appl., 23 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066678	A2	20020829	WO 2002-GB759	20020220
WO 2002066678	A3	20030530		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
 TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-4163 A 20010220

AB A method of uniquely identifying an object by labeling it with a DNA
 sequence is described. The DNA sequence has a terminal region including a
 moiety that can be used to attach it to a substrate. Adjacent to this is
 a sequence by which the DNA can be released from the substrate, such as a
 restriction enzyme cleavage site. The remainder of the DNA is the unique
 identifier that includes a pair of primer binding sites sepd. by a defined
 and unique DNA sequence. The DNA may also contain base analogs or have a
 modified backbone that will prevent degrdn. of the label by nucleases.
 The DNA may also be single-stranded with the
 immobilization region in the loop of a stem loop structure. The partially
 double stranded region may serve as a primer for an initial amplification.
 Amplification and sequencing of the unique sequence identifier can be used
 to demonstrate ownership.

IT 15181-41-60, Thiophosphate, nucleic acid conjugates
 RL: TEM (Technical or engineered material use); USES (Uses)
 (for immobilization of oligonucleotide label; defined DNA
 sequences amplifiable with universal primer pair for use in labeling
 materials for identification)

=> d ibib abs hitrn 10

L75 ANSWER 10 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2002:575095 HCAPLUS
 DOCUMENT NUMBER: 137:106042
 TITLE: Nuclease-based method for detecting and quantitating
 oligonucleotides
 INVENTOR(S): Yu, Zhengrong; Baker, Brenda F.; Wu, John
 PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 48 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059137	A1	20020801	WO 2001-US49702	20011023

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
 RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
 UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1337547 A1 20030827 EP 2001-994359 20011023

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2000-705587 A 20001103
 WO 2001-US49702 W 20011023

AB The invention concerns a method for quantitating an oligonucleotide in a sample of bodily fluid and/or ext. is provided. The method comprises contacting an oligonucleotide with a probe comprising a detectable marker and a binding moiety; placing the fluid or ext. in contact with a solid support to which a binding partner of the binding moiety is attached; contacting the fluid or ext. with a single-strand specific nuclease to degrade probe which is not hybridized to the oligonucleotide; and detecting a label assocd. with the marker. The method provides or the detection and/or localization of oligonucleotides, including administered modified oligonucleotides, for therapeutic and/or pharmacokinetic purposes.

IT 15181-41-6, Phosphorothioate

RL: PRP (Properties)
 (nuclease-based method for detecting and quantitating oligonucleotides)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitrn 11

L75 ANSWER 11 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:522052 HCAPLUS

DOCUMENT NUMBER: 137:89420

TITLE: Single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA)

INVENTOR(S): Bandaru, Rajanikanth; Kumar, Gyanendra

PATENT ASSIGNEE(S): Molecular Staging, Inc., USA

SOURCE: PCT Int. Appl., 90 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053780	A2	20020711	WO 2002-US5	20020104
WO 2002053780	A3	20030522		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003044794 A1 20030306 US 2001-910372 20010720

US 6635425 B2 20031021

EP 1347988 A2 20031001 EP 2002-705674 20020104

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2003207323 A1 20031106 US 2003-465759 20030619

PRIORITY APPLN. INFO.: US 2001-259918P P 20010105

US 2001-910372 A 20010720

WO 2002-US5 W 20020104

AB The present invention provides a novel method for ligation of oligonucleotides contg. 5'-phosphorothioates on complementary templates by the action of DNA ligases. This reaction is readily applied to the synthesis of a single stranded circular DNA contg. a phosphorothioate directed ligation reaction by ATP dependent DNA ligase reaction is similar to conventional 5'-phosphate ligation. The utility of enzymic ligation in

probing specific sequences of DNA is also described. The present invention also provides a novel non-enzymic ligation of 5'-phosphorothioates that has been applied to the synthesis of single strand phosphorothioate and phosphate circular DNA. A process for detecting the presence of a mismatch in an otherwise complementary pair of oligonucleotides is disclosed using an enzyme-based technique which shows the presence of a mismatch by failing to form a ligated single stranded DNA circle that can optionally be amplified using std. methods of rolling circle amplification.

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L75 ANSWER 11 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN
 IC ICM C12Q001-68
 CC 3-1 (Biochemical Genetics)
 Section cross-reference(s): 13
 ST genotyping SNP single nucleotide polymorphism DNA high throughput assay;
 human genomic DNA SNP genotyping rolling circle amplification method;
 oligonucleotide rolling circle amplification nucleic acid
 IT Thermus thermophilus
 (DNA ligase from; single-stranded circular oligonucleotide probes for
 detection of polymorphisms in nucleic acids by rolling-circle
 amplification (RCA))
 IT Escherichia coli
 Rhodothermus marinus
 Thermus scotoductus
 (DNA ligase; single-stranded circular oligonucleotide probes for
 detection of polymorphisms in nucleic acids by rolling-circle
 amplification (RCA))
 IT Bacillus phage .phi.29
 Coliphage T4
 Coliphage T7
 (DNA polymerase; single-stranded circular oligonucleotide probes for
 detection of polymorphisms in nucleic acids by rolling-circle
 amplification (RCA))
 IT Primers (nucleic acid)
 RL: ARG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties);
 ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (DNA, Amplifluor, fluorescent labeled; single-stranded circular
 oligonucleotide probes for detection of polymorphisms in nucleic acids
 by rolling-circle amplification (RCA))
 IT Genome
 (DNA; single-stranded circular oligonucleotide probes for detection of
 polymorphisms in nucleic acids by rolling-circle amplification (RCA))
 IT Alleles
 (biallelic SNPs; single-stranded circular oligonucleotide probes for
 detection of polymorphisms in nucleic acids by rolling-circle
 amplification (RCA))
 IT RNA
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (bridging oligonucleotides contg.; single-stranded circular
 oligonucleotide probes for detection of polymorphisms in nucleic acids
 by rolling-circle amplification (RCA))
 IT Peptides, biological studies
 Primers (nucleic acid)
 Proteins
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (closed circle oligonucleotides conjugates to; single-stranded circular
 oligonucleotide probes for detection of polymorphisms in nucleic acids
 by rolling-circle amplification (RCA))
 IT Human
 (genomic DNA polymorphisms; single-stranded circular oligonucleotide
 probes for detection of polymorphisms in nucleic acids by
 rolling-circle amplification (RCA))
 IT Conformation
 (hairpin loop, in oligonucleotide; single-stranded circular
 oligonucleotide probes for detection of polymorphisms in nucleic acids
 by rolling-circle amplification (RCA))
 IT Enzymes, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (mRNA-capping, single-stranded circular oligonucleotides synthesis
 using; single-stranded circular oligonucleotide probes for detection of
 polymorphisms in nucleic acids by rolling-circle amplification (RCA))
 IT Glass, uses

- Plastics, uses
 RL: DEV (Device component use); USES (Uses)
 (oligonucleotide attached to solid support contg.; single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT Deoxyribonucleotides
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (open circle oligonucleotides and bridging oligonucleotides contg.; single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT DNA
 RL: ARG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (primer, Amplifluor, fluorescent labeled; single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT Nucleic acid amplification (method)
 (rolling circle amplification; single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT Genetic polymorphism
 (single nucleotide; single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT Genotyping (method)
 Nucleic acid hybridization
 (single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT DNA
 RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT Probes (nucleic acid)
 RL: ARG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT Oligonucleotides
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
 (single-stranded circular, bridging, synthesis of; single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT Phosphorothioate oligonucleotides
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
 (single-stranded circular, synthesis of; single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT 9015-85-4, DNA ligase
 RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (E. coli, Thermus, Rhodothermus marinus, T4, single-stranded circular oligonucleotides synthesis using; single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT 9012-90-2D, DNA polymerase, Klenow fragment
 RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (E. coli, phage T4 or T7, .phi.29, rolling circle amplification using; single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT 56-65-5, ATP, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (as DNA ligase cofactor; single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT 7786-30-3, Magnesium chloride (MgCl₂), biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (in ligation reaction buffer; single-stranded circular oligonucleotide

- probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT 25952-53-8, EDC
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(in single-stranded circular oligonucleotide synthesis; single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT 9037-46-1, Exonuclease I
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(ligation reaction products treated with; single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT 7704-34-9, Sulphur, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(of 5'phosphorothioate group not used as bridging atom for single-stranded circular oligonucleotide synthesis; circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT 9012-90-2, Taq DNA ligase 37259-52-2, Ampligase 37353-39-2
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(single-stranded circular oligonucleotides synthesis using; single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))
- IT 440688-20-0 440688-21-1 440688-22-2 440688-23-3 440688-24-4, 5:
PN: W002053780 SEQID: 5 unclaimed DNA 440688-25-5, 6: PN: W002053780
SEQID: 6 unclaimed DNA 440688-26-6, 7: PN: W002053780 SEQID: 7 unclaimed
DNA 440688-27-7, 8: PN: W002053780 SEQID: 8 unclaimed DNA 440688-28-8
440688-29-9 440688-30-2 440688-31-3 440688-32-4 440688-33-5
440688-34-6 440688-35-7 440688-36-8 440688-37-9 440688-38-0
440688-39-1 440688-40-4
RL: PRP (Properties)
(unclaimed nucleotide sequence; single-stranded circular oligonucleotide probes for detection of polymorphisms in nucleic acids by rolling-circle amplification (RCA))

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L75 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:90226 HCAPLUS
DOCUMENT NUMBER: 136:145278
TITLE: Use of modified oligonucleotide to down-regulate gene expression
INVENTOR(S): Agrawal, Sudhir; Diasio, Robert B.; Zhang, Zhang
PATENT ASSIGNEE(S): Hybridon, Inc., USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008420	A2	20020231	WO 2001-US18338	20010606
WO 2002008420	A3	20021017		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6608035	B1	20030819	US 2000-587934	20000606
PRIORITY APPLN. INFO.:				
			US 2000-587934	A 20000606
			US 1994-328520	A2 19941025
			US 1996-709910	B2 19960909
			US 1996-758005	B1 19961127
AB Disclosed is a method of down-regulating the expression of a gene in an animal, wherein a pharmacol. formulation comprising a chimeric oligonucleotide complementary to the gene is orally administered to an animal. The oligonucleotide administered has at least one				

phosphorothioate internucleotide linkage and at least one alkylphosphonate, phosphorodithioate, alkylphosphonothioate, phosphoramidate, phosphoramidite, phosphate ester, carbamate, carbonate, phosphate triester, acetamidate, or carboxymethyl ester internucleotide linkage.

- IT 15181-41-6, Phosphorothioate
 RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses) (internucleoside linkage; use of modified oligonucleotide to down-regulate gene expression)
- => d ind 12
- L75 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN
- IC ICM C12N015-11
 ICS C07H021-00; A61K031-7125; A61P025-28; A61P031-00; A61P033-00
- CC 1-12 (Pharmacology)
 Section cross-reference(s): 3, 14
- ST modified oligonucleotide drug gene expression regulation
- IT Lymphoma
 (Burkitt's; use of modified oligonucleotide to down-regulate gene expression)
- IT Trypanosoma cruzi
 (Chagas' disease from; use of modified oligonucleotide to down-regulate gene expression)
- IT Leukemia
 (T-cell, adult; use of modified oligonucleotide to down-regulate gene expression)
- IT Oligonucleotides
 RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (acetamidate linked; use of modified oligonucleotide to down-regulate gene expression)
- IT Ameba
 (amebiasis; use of modified oligonucleotide to down-regulate gene expression)
- IT Gene
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (cellular, oligonucleotide is complementary to; use of modified oligonucleotide to down-regulate gene expression)
- IT Disease, animal
 (cryptosporidiosis, trichomoniasis; use of modified oligonucleotide to down-regulate gene expression)
- IT Gene
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (expression; use of modified oligonucleotide to down-regulate gene expression)
- IT Filaria
 (filariasis; use of modified oligonucleotide to down-regulate gene expression)
- IT Disease, animal
 (foot-and-mouth disease; use of modified oligonucleotide to down-regulate gene expression)
- IT Pathogen
- Virus
 (gene, oligonucleotide is complementary to; use of modified oligonucleotide to down-regulate gene expression)
- IT Intestine, disease
 (giardiasis; use of modified oligonucleotide to down-regulate gene expression)
- IT Human herpesvirus 3
 (herpes zoster from; use of modified oligonucleotide to down-regulate gene expression)
- IT Ascarid
 (infestation with, Ascariasis; use of modified oligonucleotide to down-regulate gene expression)
- IT Pharynx, neoplasm
 (nasopharynx, carcinoma; use of modified oligonucleotide to down-regulate gene expression)
- IT Human herpesvirus
 (oral and genital; use of modified oligonucleotide to down-regulate gene expression)
- IT Drug delivery systems
 (oral; use of modified oligonucleotide to down-regulate gene expression)
- IT Wart

- (papilloma; use of modified oligonucleotide to down-regulate gene expression)
- IT Oligonucleotides
 RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (phosphoramidite linked; use of modified oligonucleotide to down-regulate gene expression)
- IT Schistosoma
 (schistosomiasis from; use of modified oligonucleotide to down-regulate gene expression)
- IT Toxoplasma gondii
 (toxoplasmosis from; use of modified oligonucleotide to down-regulate gene expression)
- IT AIDS (disease)
 Alzheimer's disease
 Blood plasma
 Drug metabolism
 Hepatitis
 Influenza
 Malaria
 Mammalia
 Parasite
 Pneumocystis
 Trichinella
 Trichomonacides
 (use of modified oligonucleotide to down-regulate gene expression)
- IT Proteins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (use of modified oligonucleotide to down-regulate gene expression)
- IT Oligonucleotides
 Phosphorothioate oligonucleotides
 RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (use of modified oligonucleotide to down-regulate gene expression)
- IT Human herpesvirus 3
 (varicella from; use of modified oligonucleotide to down-regulate gene expression)
- IT Papilloma
 (warts; use of modified oligonucleotide to down-regulate gene expression)
- IT Fever and Hyperthermia
 (yellow; use of modified oligonucleotide to down-regulate gene expression)
- IT 463-77-4, Carbamic acid, biological studies 993-13-5 3812-32-6, Carbonate, biological studies 7664-38-2D, Phosphoric acid, triesters, biological studies 13598-36-2D, Phosphonic acid, alkyl 15181-41-6, Phosphorothioate 16481-04-2, Carboxy methyl ester 22638-09-1, Phosphoramidate
 RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (internucleoside linkage; use of modified oligonucleotide to down-regulate gene expression)
- IT 393599-15-0 393599-16-1 393599-17-2 393599-18-3 393599-19-4 393599-20-7 393599-21-8 393599-22-9 393599-23-0 393599-24-1 393599-25-2 393599-26-3 393599-27-4 393599-28-5 393599-29-6
 RL: PRP (Properties)
 (unclaimed nucleotide sequence; use of modified oligonucleotide to down-regulate gene expression)

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L75 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:457395 HCAPLUS

DOCUMENT NUMBER: 137:259481

TITLE: Separation of Synthetic Oligonucleotide Dithioates from Monothiophosphate Impurities by Anion-Exchange Chromatography on a Mono-Q Column

AUTHOR(S): Yang, Xianbin; Hodge, Richard P.; Luxon, Bruce A.; Shope, Robert; Gorenstein, David G.

CORPORATE SOURCE: Sealy Center for Structural Biology and Department of Human Biological Chemistry & Genetics, University of Texas Medical Branch at Galveston, TX, 77555-1157, USA

SOURCE: Analytical Biochemistry (2002), 306(1), 92-99

CODEN: ANBCA2; ISSN: 0003-2697

PUBLISHER: Elsevier Science

DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A method using a strong anion-exchange liq.-chromatog. column, Mono-Q, has been developed for high-resoln. anal. and purifn. of oligonucleotide dithioates, which were synthesized by an automated, solid-phase, phosphorothioamidite chem. High-resoln. sepn. of oligonucleotide phosphorodithioates from monothiophosphate impurities was obtained. High-resoln. sepn. was also demonstrated at pH 8. The sepn. of oligonucleotide dithioates was found to be linearly dependent on the no. of sulfurs for the same sequence length. Thiocyanate, SCN-, as eluting anion, can be used to purify oligonucleotides contg. a high percentage of phosphorodithioate linkages in lower salt concns. and provides better sepn. than chloride as eluting anion.
 IT 15181-41-6P, Phosphorothioate
 RL: BYP (Byproduct); PREP (Preparation)
 (mono-, di-, sepn. of synthetic oligonucleotide dithioates from monothiophosphate impurities by anion-exchange chromatog. on a mono-Q column)
 REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ind 13

L75 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN
 CC 9-3 (Biochemical Methods)
 Section cross-reference(s): 6
 ST monoQ column oligonucleotide dithioate chromatog purifn; monothiophosphate oligonucleotide phosphorodithioate sepn
 IT pH
 (8, sepn. at; sepn. of synthetic oligonucleotide dithioates from monothiophosphate impurities by anion-exchange chromatog. on a mono-Q column)
 IT Ion exchange chromatography
 (high-performance; sepn. of synthetic oligonucleotide dithioates from monothiophosphate impurities by anion-exchange chromatog. on a mono-Q column)
 IT Phosphorothioate oligonucleotides
 RL: PUR (Purification or recovery); PREP (Preparation)
 (sepn. of synthetic oligonucleotide dithioates from monothiophosphate impurities by anion-exchange chromatog. on a mono-Q column)
 IT 302-04-5, Thiocyanate, uses
 RL: NUU (Other use, unclassified); USES (Uses)
 (eluting anion of; sepn. of synthetic oligonucleotide dithioates from monothiophosphate impurities by anion-exchange Chromatog. on a mono-Q column)
 IT 15181-41-6P, Phosphorothioate
 RL: BYP (Byproduct); PREP (Preparation)
 (mono-, di-, sepn. of synthetic oligonucleotide dithioates from monothiophosphate impurities by anion-exchange chromatog. on a mono-Q column)
 IT 131159-51-8, Mono Q HR 10/10
 RL: NUU (Other use, unclassified); USES (Uses)
 (sepn. of synthetic oligonucleotide dithioates from monothiophosphate impurities by anion-exchange chromatog. on a mono-Q column)

=> d ibib abs hitrn 14

L75 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 2001:868734 HCAPLUS
 DOCUMENT NUMBER: 136:1591
 TITLE: Genotyping methods to detect DNA sequence polymorphisms and haplotypes
 INVENTOR(S): Stanton, Vincent P., Jr.
 PATENT ASSIGNEE(S): Variagenics, Inc., USA
 SOURCE: PCT Int. Appl., 166 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001090419	A2	20011129	WO 2001-US16577	20010523
WO 2001090419	A3	20030710		

W: AE, AG, AL, AM, AT, AU, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
 HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
 LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
 RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6475736 B1 20021105 US 2000-696998 20001025

PRIORITY APPLN. INFO.:

US 2000-206613P P 20000523

US 2000-696998 A2 20001025

US 2000-697013 A2 20001025

US 2000-697028 A2 20001025

AB Methods for detg. genotypes and haplotypes of genes are claimed. Also described are single nucleotide polymorphisms (SNPs) and haplotypes in the ApoE gene and their use in methods of this invention. Methods of the invention involve allele enrichment methods such as allele capture, allele-specific amplification, and allele-specific restriction endonuclease digestion. Allele capture means phys. sepn. of either single-stranded or double-stranded DNA. This can be accomplished by protein or nucleic acid reagents, such as disabled restriction enzymes, zinc-finger DNA-binding proteins, and covalent crosslinking agents, which have affinity for specific alleles. The captured complexes are then sepd. from the nucleic acid mixt. by reagents such as antibody-coated beads or streptavidin. Allele-specific amplification can be accomplished by strand obstruction, such as formation of stable secondary structures, or modified primers such as covalently crosslinkable primers. Lastly, allele-specific restriction methods for genotyping can be accomplished by triplex-mediated protection, primer-mediated creation of polymorphic restriction sites, and other variations, followed by amplification, direct nucleotide sequencing, or capture and size or sequence anal. Allele-specific primers were designed to det. haplotypes of nucleotide 186 T/C and 597 A/G polymorphisms in the dihydropyrimidine dehydrogenase gene. The primers are allele-specific because they induce hairpin loop formation when the "correct" nucleotide is present at the polymorphic site. The hairpin loop structure inhibits annealing of new primers and further amplification. PCR products were digested with BsrDI restriction endonuclease and analyzed by agarose gel electrophoresis. A T/C SNP at genomic site 21250 in the human ApoE gene results in a cysteine to arginine substitution at position 176 of the ApoE protein. For genotyping the T/C SNP, a loop primer and reverse primer were designed to amplify the target and introduce FokI and FspI restriction enzyme cleavage sites. Digestion with FokI and FspI produced allele-specific DNA fragments which were sequenced by mass spectrometry. Fourteen polymorphic sites for the ApoE gene and exptl. derived haplotypes for some or all of these polymorphisms are provided.

=> d ind 14

L75 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN

IC ICM C12Q001-68

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 9, 13

ST genotyping polymorphism haplotype allele DNA binding complex restriction endonuclease; human gene ApoE SNP genotype haplotype PCR sequence analysis

IT Gene, animal

RL: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(APOE; genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Quaternary structure

(DNA triplex, allele-specific; genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Ligands

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(DNA-binding; genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Primers (nucleic acid)

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(DNA; genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Enzymes, biological studies

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(RecA; genotyping methods to detect DNA sequence polymorphisms and

haplotypes)

IT Molecular association
(allele-specific DNA-binding; genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Hydrogen bond
(allele-specific; genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT RNA
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(aptamer; genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Peptide nucleic acids
Proteins
Transcription factors
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(biotinylated or immobilized; genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT DNA
RL: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(double-stranded; genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Alleles
Crosslinking
Genotypes
Genotyping (method)
Immunoassay
Nucleic acid amplification (method)
PCR (polymerase chain reaction)
RFLP (restriction fragment length polymorphism)
(genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Gene, animal
cDNA
RL: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Oligonucleotides
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Peptide nucleic acids
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Phosphorothioate oligonucleotides
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Primers (nucleic acid)
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Proteins
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Transcription factors
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Peptides, biological studies
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(histidine-contg., ligand tag; genotyping methods to detect DNA sequence polymorphisms and haplotypes)

IT Oligonucleotides
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)

- (immobilized; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT Oligonucleotides
 - RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 - (labeled, biotinylated; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT Magnetic particles
 - (ligand tag; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT Antibodies
 - Avidins
 - RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 - (ligand tag; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT Conformation
 - (loop, nucleic acid, D-loop, allele-specific; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT DNA sequence analysis
 - (mass spectrometric; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT Nucleic acid bases
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (mass-modified; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT Imaging
 - (optical mapping; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT Nucleic acid bases
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (pairing, allele-specific; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT DNA
 - RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 - (primer; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT Genetic element
 - RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 - (restriction endonuclease cleavage site; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT Polyamides, biological studies
 - RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 - (sequence-specific DNA-binding; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT Genetic polymorphism
 - (single nucleotide; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT DNA
 - RL: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 - (single-stranded; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT Separation
 - (size selection; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT Immunoassay
 - (solid-phase; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT Proteins
 - RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 - (zinc finger-contg., biotinylated or immobilized; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT Proteins
 - RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 - (zinc finger-contg.; genotyping methods to detect DNA sequence polymorphisms and haplotypes)
- IT 9012-90-2, DNA polymerase
 - RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 - (T4 and I, exonuclease; genotyping methods to detect DNA sequence polymorphisms and haplotypes)

- IT 66-97-7, Psoralen 22542-10-5D, complexes, biological studies
146237-51-6 146237-52-7 146237-53-8
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST
(Analytical study); BIOL (Biological study); USES (Uses)
(crosslinking agent; genotyping methods to detect DNA sequence
polymorphisms and haplotypes)
- IT 9026-89-5, Dihydropyrimidine dehydrogenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gene for; genotyping methods to detect DNA sequence polymorphisms and
haplotypes)
- IT 9037-44-9, Escherichia coli exonuclease III 9075-08-5, Restriction
endonuclease 37228-74-3, Exonuclease 37367-70-7, Lambda exonuclease
58513-62-5, Nuclease, bacteriophage T7 exodeoxyribo-
81295-34-3, Restriction endonuclease PvuII 81458-03-9, Restriction
endonuclease FokI 85340-94-9, Bal31 exonuclease 92228-44-9,
Restriction endonuclease NcoI 103780-20-7, NotI restriction endonuclease
107824-63-5 135340-89-5, Restriction endonuclease N.BstNBI
174632-11-2, Restriction endonuclease BsgI 189088-83-3, Restriction
endonuclease BsrDI
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST
(Analytical study); BIOL (Biological study); USES (Uses)
(genotyping methods to detect DNA sequence polymorphisms and
haplotypes)
- IT 58-85-5, Biotin 7440-02-0, Nickel, biological studies 9013-20-1,
Streptavidin
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST
(Analytical study); BIOL (Biological study); USES (Uses)
(ligand tag; genotyping methods to detect DNA sequence polymorphisms
and haplotypes)
- IT 9025-82-5, Phosphodiesterase
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST
(Analytical study); BIOL (Biological study); USES (Uses)
(snake venom type I; genotyping methods to detect DNA sequence
polymorphisms and haplotypes)

=> d ibib abs hitrn 15

L75 ANSWER 15 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:115526 HCAPLUS
DOCUMENT NUMBER: 130:292382
TITLE: High sequence fidelity in a non-enzymic DNA
autoligation reaction
AUTHOR(S): Xu, Yanzheng; Kool, Eric T.
CORPORATE SOURCE: Department of Chemistry, University of Rochester,
Rochester, NY, 14627, USA
SOURCE: Nucleic Acids Research (1999), 27(3), 875-881
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The success of oligonucleotide ligation assays in probing
specific sequences of DNA arises in large part from high enzymic
selectivity against base mismatches at the ligation junction. We describe
here a study of the effect of mismatches on a new non-enzymic,
reagent-free method for ligation of oligonucleotides. In this
approach, two oligonucleotides bound at adjacent sites on a
complementary strand undergo autoligation by displacement of a 5'-end
iodide with a 3'-phosphorothioate group. The data show that
this ligation proceeds somewhat more slowly than ligation by T4 ligase,
but with substantial discrimination against single base mismatches both at
either side of the junction and a few nucleotides away within one of the
oligonucleotide binding sites. Selectivities of >100-fold against
a single mismatch are obsd. in the latter case. Expts. at varied concns.
and temps. are carried out both with the autoligation of two adjacent
linear oligonucleotides and with intramol. autoligation to yield
circular "padlock" DNAs. Application of optimized conditions to
discrimination of an H-ras codon 12 point mutation is demonstrated with a
single-stranded short DNA target.

- IT 15181-41-6, Phosphorothioate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(autoligation by displacement of a 5'-end iodide with a 3'-
phosphorothioate group; high sequence fidelity in a non-enzymic
DNA autoligation reaction)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ind 15

L75 ANSWER 15 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN
 CC 3-4 (Biochemical Genetics)
 Section cross-reference(s): 6, 9
 ST nonenzymic DNA autoligation reaction high sequence fidelity
 IT Codons
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (12, application of optimized conditions to discrimination of an H-ras
 codon 12 point mutation is demonstrated; high sequence fidelity in a
 non-enzymic DNA autoligation reaction)
 IT DNA
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological
 process); BSU (Biological study, unclassified); BIOL (Biological study);
 PROC (Process)
 (autoligation; high sequence fidelity in a non-enzymic DNA autoligation
 reaction)
 IT Mutation
 (base-mismatching, ligation proceeds more slowly than ligation by T4
 ligase, but with discrimination against single base mismatches; high
 sequence fidelity in a non-enzymic DNA autoligation reaction)
 IT Gene, animal
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (c-Ha-ras, application of optimized conditions to discrimination of an
 H-ras codon 12 point mutation is demonstrated; high sequence fidelity
 in a non-enzymic DNA autoligation reaction)
 IT DNA
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
 BIOL (Biological study); OCCU (Occurrence)
 (circular, autoligation of two adjacent linear oligonucleotides
 and with intramol. autoligation to yield circular "padlock" DNAs; high
 sequence fidelity in a non-enzymic DNA autoligation reaction)
 IT Mutation
 (point, application of optimized conditions to discrimination of an
 H-ras codon 12 point mutation is demonstrated; high sequence fidelity
 in a non-enzymic DNA autoligation reaction)
 IT 15181-41-6, Phosphorothioate
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); BIOL (Biological study)
 (autoligation by displacement of a 5'-end iodide with a 3'-
 phosphorothioate group; high sequence fidelity in a non-enzymic
 DNA autoligation reaction)
 IT 20461-54-5, Iodide, biological studies
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (autoligation by displacement of a 5'-end iodide with a 3'-
 phosphorothioate group; high sequence fidelity in a non-enzymic
 DNA autoligation reaction)

=> d ibib abs hitrn 16

L75 ANSWER 16 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN
 ACCESSION NUMBER: 1994:623647 HCAPLUS
 DOCUMENT NUMBER: 121:223647
 TITLE: Enzymic preparation of single-stranded DNA containing
 nuclease-resistant modified nucleotides using
 phosphorothioate-containing primers
 INVENTOR(S): Nikiforov, Theo; Knapp, Michael R.
 PATENT ASSIGNEE(S): Molecular Tool, Inc., USA
 SOURCE: PCT Int. Appl., 57 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 9
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9416090	A1	19940721	WO 1994-US771	19940118
W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5518900	A	19960521	US 1993-155746	19931123
AU 9461262	A1	19940815	AU 1994-61262	19940118

AU 674211 B2 19961212
 EP 679190 A1 19951102 EP 1994-907855 19940118
 EP 679190 B1 20030502
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
 JP 08505535 T2 19960618 JP 1994-516386 19940118
 JP 3330946 B2 20021007
 AT 239090 E 20030515 AT 1994-907855 19940118
 PRIORITY APPLN. INFO.: US 1993-5061 A 19930115
 US 1993-155746 A 19931123
 WO 1994-US771 W 19940118

AB A method for generating single-stranded nucleic acid mols. that contain nuclease-resistant modified nucleotides and so are resistant to 5'.fwdarw.3'-exonucleases are described. The method involves synthesizing the nucleic acid by primer extension using **phosphorothioate** -contg. primers. A pair of primers with one of them having a phosphorothioate-rich 5'-region and the other not contg. **phosphorothioate** nucleotides are used to amplify the target sequence. The amplification products are then digested with a 5'.fwdarw.3'-nuclease with the hydrolysis of all of the nucleic acids present except for the amplification products contg. the phosphorothioate-rich primer. These products can be used in DNA sequencing and in the detn. of genetic polymorphism, esp. single base polymorphisms. If the phosphorothioates are placed at the 3'-end of the primer, then any residual primers in the reaction can be hydrolyzed with a 5'.fwdarw.3'-nuclease to prevent further amplification.

=> d ind 16

L75 ANSWER 16 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN
 IC ICM C12P019-34
 CC 3-1 (Biochemical Genetics)
 ST nuclease resistant single stranded DNA
 IT Deoxyribonucleic acid sequence determination
 Polymerase chain reaction
 (enzymic prepn. of single-stranded DNA contg. nuclease-resistant modified nucleotides using **phosphorothioate**-contg. primers)
 IT Genetic polymorphism
 (single base, detn. of; enzymic prepn. of single-stranded DNA contg. nuclease-resistant modified nucleotides using **phosphorothioate** -contg. primers)
 IT Deoxyribonucleic acids
 RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
 (single-stranded; enzymic prepn. of single stranded DNA contg. nuclease-resistant modified nucleotides using **phosphorothioate**-contg. primers)
 IT Nucleotides, biological studies
 RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (oligo-, deoxyribo-, thiophosphate-linked, primers; enzymic prepn. of single-stranded DNA contg. nuclease-resistant modified nucleotides using **phosphorothioate** -contg. primers)
 IT Deoxyribonucleic acids
 RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
 (thiophosphate-linked, single-stranded, nuclease resistant; enzymic prepn. of single-stranded DNA contg. nuclease-resistant modified nucleotides using **phosphorothioate**-contg. primers)
 IT 79121-99-6, 5'.fwdarw.3'-Exonuclease
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (phage T6 or .lambda.; enzymic prepn. of single-stranded DNA contg. nuclease-resistant modified nucleotides using **phosphorothioate**-contg. primers)

=> d ibib abs hitrn 17

L75 ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN
 ✓ ACCESSION NUMBER: 1992:229075 HCAPLUS
 DOCUMENT NUMBER: 116:229075
 TITLE: **Phosphorothioate-based site-directed mutagenesis for single-stranded vectors**
 AUTHOR(S): Sayers, Jon R.; Eckstein, Fritz

CORPORATE SOURCE: Abt. Chem., Max Planck Inst. Exp. Med., Heidelberg,
D-6900/1, Germany

SOURCE: Directed Mutagen. (1991), 49-69. Editor(s):
McPherson, M. J. IRL: Oxford, UK.
CODEN: 57RUAL

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review with 22 refs. The **phosphorothioate**-based **oligonucleotide**-directed mutagenesis method is based on the observation that certain restriction endonucleases are incapable of hydrolyzing **phosphorothioate** internucleotidic linkages. Thus, double-stranded DNA contg. **phosphorothioate** linkages in one strand only may be nicked in the non-substituted strand. In this mutagenesis procedure the mismatch **oligonucleotide** primer is annealed to the (+)strand of a **single-stranded** circular phage DNA. The primer is extended by a polymn. reaction in which one of the natural deoxynucleoside triphosphates is replaced by the corresponding deoxynucleotide 5'-O-(1-thiotriphosphate), dNTP.alpha.S. Thus, **phosphorothioate** groups are incorporated exclusively into the (-)strand of the newly synthesized RF-IV DNA. This results in a strand asymmetry which may be exploited. The methods, scope, and limitations of the procedure are discussed.

IT 15181-41-6, **Phosphorothioate**
RL: BIOL (Biological study)
(for site-directed mutagenesis of **single-stranded** DNA vectors)

=> d ind 17

L75 ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2003 ACS on STN

CC 3-0 (Biochemical Genetics)
Section cross-reference(s): 9

ST mutagenesis site directed **phosphorothioate** review

IT Genetic vectors
(**single-stranded** DNA, site-directed **phosphorothioate**-based mutagenesis of)

IT Mutation
(site-specific, **phosphorothioate**-based, for **single-stranded** DNA vectors)

IT 15181-41-6, **Phosphorothioate**
RL: BIOL (Biological study)
(for site-directed mutagenesis of **single-stranded** DNA vectors)